REMARKS/ARGUMENTS

I. Status of the Claims and Amendments:

Claims 144, 168 and 177 have been amendment herewith. Claims 144, 147 – 148, 150 - 161, 163 – 168 and 170 – 192 are pending in the application.

II. Rejections under 35 U.S.C. §112 – Scope of Enablement

The Examiner has maintained the rejections of pages 3 – 6 of the previous office action which found in part that the specification was not enabling for regulating gene expression using any mutated steroid hormone receptor. While not acquiescing to the Examiner's prior basis of rejection, in the interests of advancing prosecution, in the last filed response the prior pending claims were amended to recite that the ligand binding domain is a mutated progesterone receptor ligand binding domain and that the mutation is in one or more of the final 54 C′ terminal amino acids of the ligand binding domain.

It now appears that the Examiner finds that the specification is not enabling for the generation of any mutation in the C′ terminal 54 amino acids of the ligand binding domain of a progesterone receptor, with the exception of the two exemplified 54 and 42 amino acid deletions. It is vigorous reasserted that undue experimentation would not be required to identify further deletions or substitutions in this region that would provide the same result as the surprising discovery of the present inventors that modification of the amino acid sequence in this region would convert an antagonist of the naturally occurring receptor into an antagonist. It is respectfully submitted that given the level of skill in the art, the claimed scope is fully enabled and to require the applicants to further narrow the scope is not justified under the enablement standard.

Furthermore, it is the Examiner's burden to clearly establish a prima facie case of lack of enablement by presenting sound scientific reason supported by references that establish a conclusion that the specification is not enabling. References submitted in the prior office action related to glucocorticoid and estrogen receptor mutations, not progesterone receptor mutations.

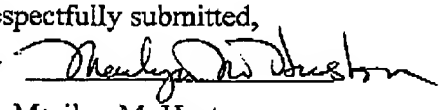
The present inventors found that C′ terminal mutations to the progesterone receptor ligand binding domain actually abolished progesterone binding. The inventors also found that, based on the fact that deletion of as much as 54 C′ terminal amino acids did not affect antiprogestin binding

and in fact allowed antiprogestins to have agonistic effect, that the region responsible for antiprogestin binding was necessarily upstream of the mutated region. Using these concrete endpoints, it would be straightforward in accordance with the high level of skill in the art to generate other mutations in the C' terminal region that destroyed progesterone binding while retaining the antiprogestin effect. Given the high level of skill in the art, routine experimentation would be sufficient to make further useful mutations given the discovery as disclosed.

Claims 144, 168 and 177 have been amended in an attempt to clarify that a target gene controlled by specific promoter would be expressed as a consequence of ligand administration in an animal expressing a molecular switch that has a DNA binding domain specific for the promoter.

Conclusion

For the reasons stated herein, the Applicant respectfully submits that independent claims 144, 168 and 177 are allowable and that the dependent claims are, in turn, also allowable. Applicant respectfully requests allowance of the claims at an early date. The Commissioner is authorized to charge any additional fees incurred in this application or credit any overpayment to Deposit Account No. 50-1922. Should the Examiner have any questions, please do not hesitate to call Applicant's attorney at 832-446-2421.

Respectfully submitted,
By 

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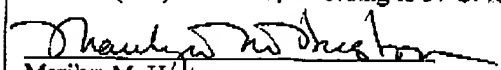

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